

Amendment Under 37 C.F.R. §1.312

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Applicant(s): PARTHASARATHY et al.

Serial No.: 10/027,222

Confirmation No.: 9052

Filed: 20 December 2001

For: METHODS AND DEVICES FOR REMOVAL OF ORGANIC MOLECULES FROM BIOLOGICAL MIXTURES USING ANION EXCHANGE

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### Amendments to the Claims

This listing of claims replaces all prior versions, and listings, of claims in the above-identified application:

1. **(Previously Presented)** A method of removing small negatively charged organic molecules from a biological sample mixture, the method comprising:

providing a device comprising a plurality of process arrays, wherein each process array of the plurality of process arrays comprises:

a plurality of process chambers, each of the process chambers defining a volume for containing a biological sample mixture; and

at least one distribution channel connecting the plurality of process chambers of the array; wherein at least one of the process arrays comprises a surface comprising an anion exchange material partially coated with a negatively charged polymer;

providing a biological sample mixture comprising small negatively charged organic molecules having a molecular weight of less than about 6,000; wherein the biological sample mixture is selected from the group consisting of a nucleic acid amplification reaction mixture and a nucleic acid labeling reaction mixture; and

contacting the biological sample mixture with the surface comprising the anion exchange material to remove at least a portion of the small negatively charged organic molecules from the biological sample mixture.

2. **(Previously Presented)** A method of removing small negatively charged organic molecules from a biological sample mixture, the method comprising:

providing a device comprising a plurality of process arrays, wherein each process array of the plurality of process arrays comprises:

a plurality of process chambers, each of the process chambers defining a volume for containing a biological sample mixture; and

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at least one distribution channel connecting the plurality of process chambers of the array; wherein at least one of the process arrays comprises a surface comprising an anion exchange material partially coated with a negatively charged polymer; providing a biological sample mixture; and contacting the biological sample mixture with the surface comprising an anion exchange material partially coated with a negatively charged polymer to remove at least a portion of the small negatively charged organic molecules from the biological sample mixture.

3. **(Original)** The method of claim 2 wherein the negatively charged polymer is a polyelectrolyte.
4. **(Original)** The method of claim 3 wherein the negatively charged polyelectrolyte is selected from the group consisting of a polystyrene sulfonic acid, polyvinyl phosphonic acid, polyvinyl boric acid, polyvinyl sulfonic acid, polyvinyl sulfuric acid, polystyrene phosphonic acid, polyacrylic acid, polymethacrylic acid, lignosulfonate, carrageenan, heparin, chondroitin sulfate, salts thereof, and mixtures thereof.
5. **(Original)** The method of claim 2 wherein the anion exchange material comprises quaternized nitrogen.
6. **(Original)** The method of claim 2 wherein the biological sample mixture is a nucleic acid sequencing reaction mixture.
7. **(Original)** The method of claim 6 wherein the small negatively charged organic molecules are selected from the group consisting of dye-labeled terminators, primers, degraded dye molecules, deoxynucleotide triphosphates, and mixtures thereof.

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8. **(Original)** The method of claim 7 wherein the small negatively charged organic molecules comprise dye-labeled terminators.
9. **(Original)** The method of claim 8 wherein the dye-labeled terminators are selected from the group consisting of dideoxynucleotide triphosphates, dideoxynucleotide diphosphates, dideoxynucleotide monophosphates, dideoxynucleosides, and combinations thereof.
10. **(Original)** The method of claim 8 wherein contacting the biological sample mixture with the surface comprising an anion exchange material partially coated with a negatively charged polymer is carried out under conditions effective to remove substantially all the dye-labeled terminators from the biological sample mixture.
11. **(Original)** The method of claim 2 wherein the biological sample mixture is a PCR reaction mixture.
12. **(Original)** The method of claim 11 wherein the small negatively charged organic molecules are selected from the group consisting of primers, degraded dye molecules, dideoxynucleotide triphosphates, and mixtures thereof.
13. **(Original)** The method of claim 12 wherein contacting the biological sample mixture with the surface comprising an anion exchange material partially coated with a negatively charged polymer is carried out under conditions effective to remove substantially all the primers from the biological sample mixture.
14. **(Original)** The method of claim 2 wherein the small negatively charged organic molecules have a molecular weight of less than about 6,000.

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15. **(Original)** The method of claim 2 wherein contacting the biological sample mixture with the surface comprising an anion exchange material partially coated with a negatively charged polymer comprises agitating while contacting.

16. **(Previously Presented)** The method of claim 2 wherein the device is a microfluidic device.

17. **(Previously Presented)** A method of removing small negatively charged organic molecules from a biological sample mixture, the method comprising:

providing a device comprising a plurality of process arrays, wherein each process array of the plurality of process arrays comprises:

a plurality of process chambers, each of the process chambers defining a volume for containing a biological sample mixture; and

at least one distribution channel connecting the plurality of process chambers of the array; wherein at least one of the process arrays comprises a surface comprising quaternary ammonium ions partially coated with a negatively charged polyelectrolyte; providing a biological sample mixture; and

contacting the biological sample mixture with the surface comprising quaternary ammonium ions partially coated with a negatively charged polyelectrolyte to remove at least a portion of the small negatively charged organic molecules from the biological sample mixture.

18. **(Previously Presented)** A method of removing small negatively charged organic molecules from a biological sample mixture, the method comprising:

providing a device comprising a plurality of process arrays, wherein each process array of the plurality of process arrays comprises:

a plurality of process chambers, each of the process chambers defining a volume for containing a biological sample mixture; and

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at least one distribution channel connecting the plurality of process chambers of the array; wherein at least one of the process arrays comprises a surface comprising quaternary ammonium ions partially coated with a negatively charged polyelectrolyte; providing a biological sample mixture; and

contacting the biological sample mixture with the surface comprising quaternary ammonium ions partially coated with a negatively charged polyelectrolyte to remove at least a portion of the small negatively charged organic molecules from the biological sample mixture; wherein the biological sample mixture comprises a nucleic acid amplification reaction mixture.

19. **(Previously Presented)** The method of claim 18 wherein the device is a microfluidic device.

20. **(Currently Amended)** A method of removing small negatively charged organic molecules from a biological sample mixture, the method comprising:

providing a device comprising a plurality of process arrays, wherein each process array of the plurality of process arrays comprises:

a plurality of process chambers, each of the process chambers defining a volume for containing a biological sample mixture; and

at least one distribution channel connecting the plurality of process chambers of the array; wherein at least one of the process arrays comprises a surface comprising an anion exchange material partially coated with a negatively charged ~~negative~~ polymer; providing a biological sample mixture in the at least one process array, wherein the biological sample mixture comprises small negatively charged organic molecules having a molecular weight of less than about 6,000; and

transferring the biological sample mixture within the at least one process array, wherein the biological sample mixture and the surface comprising an anion exchange material remain in

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contact for a sufficient time to remove at least a portion of the small negatively charged organic molecules from the biological sample mixture.

21. **(Previously Presented)** A method of removing small negatively charged organic molecules from a biological sample mixture, the method comprising:

providing a device comprising a plurality of process arrays, wherein each process array of the plurality of process arrays comprises:

a plurality of process chambers, each of the process chambers defining a volume for containing a biological sample mixture; and

at least one distribution channel connecting the plurality of process chambers of the array; wherein at least one of the process arrays comprises a surface comprising an anion exchange material partially coated with a negatively charged polymer;

providing a biological sample mixture in the at least one process array; and

transferring the biological sample mixture within the at least one process array, wherein the biological sample mixture and the surface comprising an anion exchange material partially coated with a negatively charged polymer remain in contact for a sufficient time to remove at least a portion of the small negatively charged organic molecules from the biological sample mixture.

22. **(Original)** The method of claim 21 wherein the negatively charged polymer is a polyelectrolyte.

23. **(Original)** The method of claim 22 wherein the negatively charged polyelectrolyte is selected from the group consisting of a polystyrene sulfonic acid, polyvinyl phosphonic acid, polyvinyl boric acid, polyvinyl sulfonic acid, polyvinyl sulfuric acid, polystyrene phosphonic acid, polyacrylic acid, polymethacrylic acid, lignosulfonate, carrageenan, heparin, chondritin sulfate, salts thereof, and mixtures thereof.

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24. **(Original)** The method of claim 21 wherein the anion exchange material comprises quaternary ammonium ions.
25. **(Original)** The method of claim 21 wherein the biological sample mixture is a nucleic acid sequencing reaction mixture.
26. **(Original)** The method of claim 25 wherein the small negatively charged organic molecules are selected from the group consisting of dye-labeled terminators, primers, degraded dye molecules, deoxynucleotide triphosphates, and mixtures thereof.
27. **(Original)** The method of claim 26 wherein the small negatively charged organic molecules comprise dye-labeled terminators.
28. **(Original)** The method of claim 27 wherein the dye-labeled terminators are selected from the group consisting of dideoxynucleotide triphosphates, dideoxynucleotide diphosphates, dideoxynucleotide monophosphates, dideoxynucleosides, and combinations thereof.
29. **(Original)** The method of claim 27 wherein the biological sample mixture and the surface comprising an anion exchange material partially coated with a negatively charged polymer are contacted under conditions effective to remove substantially all the dye-labeled terminators from the biological sample mixture.
30. **(Original)** The method of claim 21 wherein the biological sample mixture is a PCR reaction mixture.

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31. **(Original)** The method of claim 30 wherein the small negatively charged organic molecules are selected from the group consisting of primers, degraded dye molecules, deoxynucleotide triphosphates, and mixtures thereof.
32. **(Original)** The method of claim 31 wherein the biological sample mixture and the surface comprising an anion exchange material partially coated with a negatively charged polymer are contacted under conditions effective to remove substantially all the primers from the biological sample mixture.
33. **(Original)** The method of claim 21 wherein the small negatively charged organic molecules have a molecular weight of less than about 6,000.
34. **(Original)** The method of claim 21 wherein the biological sample mixture and the surface comprising an anion exchange material partially coated with a negatively charged polymer are agitated while in contact.
35. **(Previously Presented)** The method of claim 21 wherein the at least one process array comprises a loading chamber and at least one process chamber.
36. **(Previously Presented)** A method of removing small negatively charged organic molecules from a biological sample mixture, the method comprising:  
providing a device comprising a plurality of process arrays, wherein each process array of the plurality of process arrays comprises:  
a plurality of process chambers, each of the process chambers defining a volume for containing a biological sample mixture; and



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at least one distribution channel connecting the plurality of process chambers of the array; wherein at least one of the process arrays comprises a surface comprising quaternary ammonium ions partially coated with a negatively charged polyelectrolyte; providing a biological sample mixture in the at least one process array; and transferring the biological sample mixture within the at least one process array, wherein the biological sample mixture and the surface comprising quaternary ammonium ions partially coated with a negatively charged polyelectrolyte remain in contact for a sufficient time to remove at least a portion of the small negatively charged organic molecules from the biological sample mixture.

37. **(Original)** The method of claim 36 wherein the biological sample mixture comprises a nucleic acid amplification reaction mixture.

38. **(Original)** The method of claim 36 wherein the biological sample mixture and the surface comprising quaternary ammonium ions partially coated with a negatively charged polyelectrolyte are agitated while in contact.

39. **(Previously Presented)** A device comprising:  
a plurality of process arrays, wherein each process array of the plurality of process arrays comprises:

a plurality of process chambers, each of the process chambers defining a volume for containing a biological sample mixture; and

at least one distribution channel connecting the plurality of process chambers of the array;

wherein at least one of the process arrays comprises a surface comprising an anion exchange material partially coated with a negatively charged polymer; and

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wherein the device is operable to remove small negatively charged organic molecules from the biological sample mixture.

40. **(Original)** The device of claim 39 further comprising a plurality of valves, wherein at least one of the valves is located along the at least one distribution channel.

41. **(Original)** The device of claim 39 wherein the plurality of process arrays comprises a plurality of independent process arrays.

42. **(Original)** The device of claim 39 wherein the plurality of process arrays are arranged radially on the device.

43. **(Canceled)**

44. **(Previously Presented)** The device of claim 39 wherein the negatively charged polymer is a polyelectrolyte.

45. **(Previously Presented)** The device of claim 39 wherein the anion exchange material, the negatively charged polymer, or both are pattern coated.

46-52. **(Canceled)**

53. **(Previously Presented)** The device of claim 44 wherein the negatively charged polyelectrolyte is selected from the group consisting of a polystyrene sulfonic acid, polyvinyl phosphonic acid, polyvinyl boric acid, polyvinyl sulfonic acid, polyvinyl sulfuric acid, polystyrene phosphonic acid, polyacrylic acid, polymethacrylic acid, lignosulfonate, carrageenan, heparin, chondritin sulfate, salts thereof, and mixtures thereof.

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54. **(Previously Presented)** The device of claim 39 wherein the anion exchange material comprises quaternized nitrogen.

55-63. **(Canceled)**

64. **(Previously Presented)** A device comprising:

a plurality of process arrays, wherein each process array of the plurality of process arrays comprises:

a plurality of process chambers, each of the process chambers defining a volume for containing a biological sample mixture; and

at least one distribution channel connecting the plurality of process chambers of the array;

wherein at least one of the process arrays comprises a surface comprising quaternary ammonium ions partially coated with a negatively charged polyelectrolyte; and

wherein the device is operable to remove small negatively charged organic molecules from the biological sample mixture.

65. **(Canceled)**